

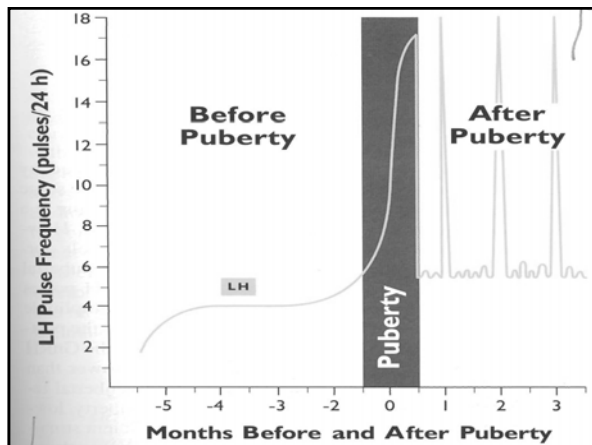
PCOS and ADOLESCENTS

Kirtly Parker Jones MD

PUBERTY

- The coordination of adrenarche and gonadarche
- The "on center" begins pulsing GnRH at night
- Gonadal steroids rise
- Destructive lesions of the hypothalamus can cause delayed puberty

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Epidemiology

- 20% of women experience abnormal bleeding during their lifetime
- Most irregular bleeding occurs within 2-3 years after menarche
 - 85% of cycles anovulatory in first year after menarche
 - [Adolescents who have not established a 24-35 day cycle by 3 years after menarche have a 50% chance of having a persistent irregular pattern]

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Anovulatory Bleeding

- Immature HPO axis
- May also be associated with
 - Sports participation
 - Stress
 - Eating disorders
 - Endocrine disorders

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Anovulatory Bleeding

- Endocrine Disorders
 - Hypothyroidism
 - Hyperthyroidism
 - Diabetes mellitus
 - Cushing syndrome

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Anovulatory Bleeding

- PCOS is a SYNDROME...not a Disease
 - 5-10% of adolescents and women of reproductive age
 - Overweight (much of the time)
 - Insulin resistance (some of the time)
 - Acanthosis nigricans (some of the time)
 - Hirsutism (some of the time)
 - Acne (some of the time)

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PCOS

- Anovulatory from puberty
- Usually <6 menses per year
- Periods are unpredictable in timing and amount
- Excessive hair growth is typical
- Most (60%-70%) are infertile
- At risk for diabetes, heart disease (?)
- At risk for sleep apnea, depression

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Prevalence

- Appears to be the same range among all races examined to date
- About 6.5% using consensus definition
- About 25% using the 2003 Rotterdam criteria (two of three):
 - Irregular periods
 - Evidence of androgen excess
 - Polycystic ovaries on ultrasound

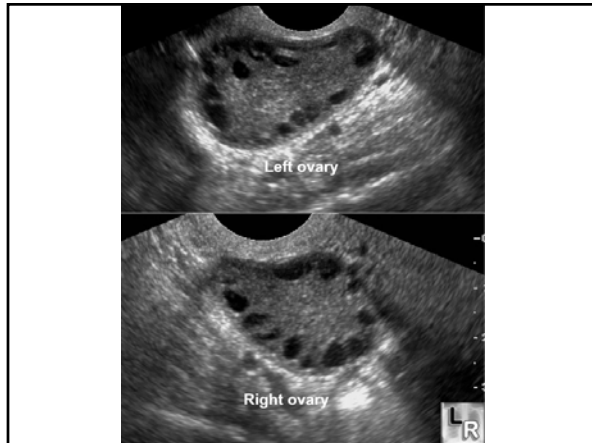
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Ultrasound Criteria....

- >12 follicles 2-9 mm in at least one of the ovaries
- Increased volume (>10cc)
- Excluded are those on OCPs and those with follicle >10mm).
- "Chain of Pearls sign" is not required

If you are using ultrasound criteria....and I don't

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Ultrasound Criteria

- Only 2 of three women with this criteria will have PCOS, and probably even fewer adolescents
- About 25% of ovulatory women have this morphology (most of our good fertile young egg donors)

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Consensus Diagnosis of PCOS

- "There is lack of consensus with even the latest consensus statement"
- Obesity is not even part of the diagnostic criteria but it does add to the clinical suspicion

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PCOS - 2008

- Hyperandrogenism –(clinical and/or biochemical)
- Ovarian dysfunction – as reflected by oligo-anovulation and/or polycystic appearing ovaries
- Exclusion of other androgen excess disorders

The Androgen Excess and PCOS Society criteria for PCOS: the Complete taskforce report. Fertil and Steril Oct 2008: 1-33, e-pub₁₈

PCOS 2008

- Clinical or biochemical signs of androgen excess are prerequisites of PCOS
- If an adolescent doesn't have hyperandrogenism, don't order ultrasound
- (I never order the ultrasound in adolescents)

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PCOS

- The diagnostic approach in adolescents should be based on history and physical exam
- Avoid numerous laboratory tests that do not contribute to clinical management

Guzick DA. Clinical Updates in Women's Health Care. ACOG 2009

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Million Dollar Workup

- TSH, Prolactin, Total testosterone (female), Free Testosterone, SHBG, androstenedione, DHEAS, Plasma free testosterone, overnight Dexamethasone Suppression test, IGF-1, 17-hydroxyprogesterone in the follicular phase, fasting insulin and glucose
- Ultrasound

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Hundred Dollar workup

- Testosterone (female) to rule out tumors (free testosterone may be elevated in the face of normal total but you know that by looking)
- Prolactin and TSH (for other causes of anovulation)
- 17-hydroxyprogesterone in the follicular phase?
- Serum glucose if clinically suspected

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PCOS and Insulin resistance (the chicken and the egg problem)

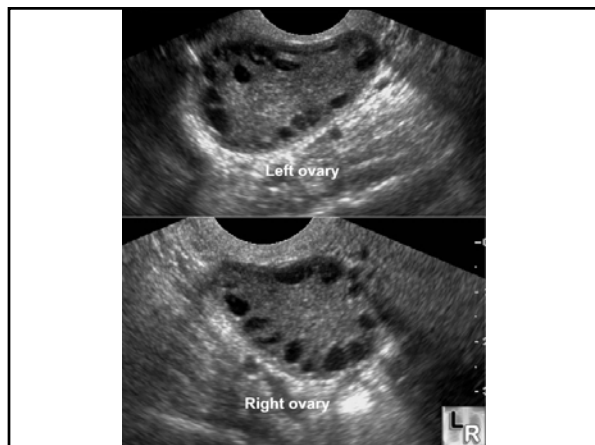
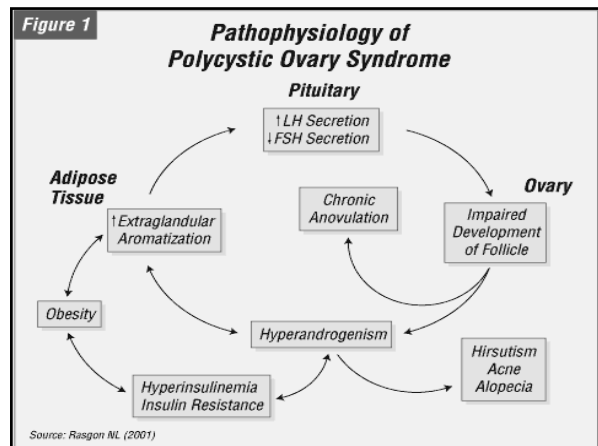
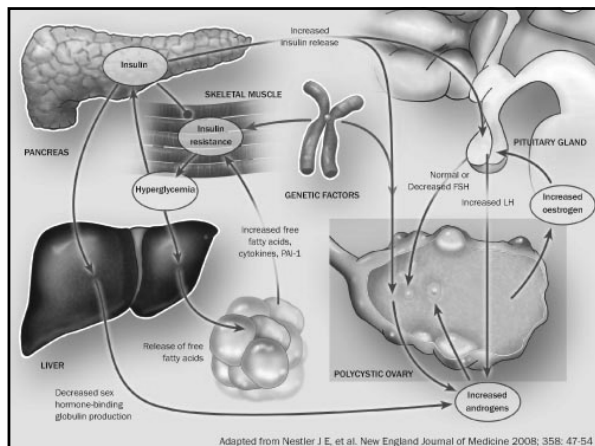
- Does obesity and insulin resistance cause PCOSor...
- Does PCOS cause insulin resistance and obesity
- Or a little of both
- (note: gastric bypass surgery "cures" PCOS in obese women)

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PCOS and Insulin resistance

- Insulin is a growth factor for the ovary
- Women who are obese sometimes have insulin resistance (it takes higher and higher insulin levels to keep glucose in the normal range)
- Fat cells are insulin resistant, but the ovaries are not

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Insulin and PCOS

- 50% of obese teens with PCOS have insulin resistance by the most sensitive tests (insulin euglycemic clamp test)
- 17% of normal weight women with PCOS have insulin resistance by the most sensitive tests

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Metformin and Adolescents with PCOS

- No real data on long term use of metformin in adolescents
- One small randomized trial in morbidly obese teens showed improvement in glucose, insulin, BMI, and menstrual cyclicity
- All effects gone within 3 months of discontinuing metformin

Ibanez L. JCEM 2001; 86: 3595-3598

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And in the Face of Clinical Suspicion...

- 24 hour urinary free cortisol to rule out Cushing's
- IGF-1 for acromegaly
- DHEAS for adrenal tumors (but I have never seen one)
- If 17-hydroxyprogesterone is very high (check your lab's normals) and you are sure it was follicular – refer

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PCOS Treatment The complicated way

- The big work up
- The big therapy
 - Metformin
 - Lifestyle modifications

Add OCPs if cycles do not regulate (and they often don't)
Repeat the big workup yearly

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PCOS Treatment The Easy Way

- Diet and exercise
- OCPs
- Check fasting glucose (or two hour post prandial....or random) if they are still gaining weight
- How do you put the fear of the mirror without creating self loathing?

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PCOS and Adolescents

- Prevent severe DUB and endometrial cancer
- Suppress ovarian androgen production and bind up the rest
- Be prepared to detect and treat diabetes

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PCOS and Adolescents

- Low dose OCPs
- Any ones will do
- Norgestimate, desogestrel, drospirnone are non androgenic progestins and have theoretical advantages

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Can't Take OCPs

- Cyclic progestins
- Androgen blocking therapies (spironolactone)

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Cosmetic therapy

- OCPs for Acne
- Laser for Hair
- eflornithine?

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Treatment for Obesity

- Diet – there is some evidence in adults that low carb is more sustainable than low fat
- A to Z weight loss Study compared:
Atkins (High protein, low carb, hi fat)
Zone (balanced carb and protein, fat)
Ornish (high carb, low fat)
Weight Watchers – (portion)

Gardiner et al: JAMA 2007;297:298-178

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Diet for PCOS

- Some websites and some science suggest low carb (or low glycemic index) high protein, high fat diets are more appropriate for PCOS
- Decrease glycemic load, decrease insulin, decrease androgens

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Treatment for Obesity

- Diet – there is evidence in adults that low carb is more sustainable than low fat
- Exercise (good luck) – 2400 calories out a week minimum
- Bariatric surgery

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Diets

- Large (811) 2 year randomized trial of various diets with counseling
- No real difference in weight loss (about 6kg at 6 months, about 3.3kg at 2 years)
- Only calories counted....
- Best predictor of success was attendance at group sessions

Sacks et al. NEJM 2009;360:859-73

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Lifestyle Changes

- Exercise (good luck) – 2400 calories out a week minimum
- Bariatric surgery is the only thing that reliably works: instant reversal of diabetes, long term success in many
- Bariatric surgery recommended for morbidly obese adolescents

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EPODE

Ensemble, prevenons l'obesite des enfants

- Community based effort to PREVENT obesity in children – started 2000
- Two small towns in France – EVERYONE got on board to change diet and exercise patterns of children
- 2007, overweight children 8% compared to 17% in surrounding towns

Romon M et al. Public Health Nutr. 2008 Dec (epub ahead of print)⁴³

Adolescents

